

# Development and evaluation of nanosized aripiprazole-loaded bioflexy films using a biopolymer from *Lagenaria siceraria* for brain delivery through orosoft palatal mucosal platform

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## Purpose

The National Institute of Mental Health estimated the global cost of mental illness to be \$6T by 2030. The purpose of the study was to deliver aripiprazole for brain targeting by suitably designing a bioflexy film for the treatment of different brain disorders.

## Materials and methods

Bioflexy films were prepared by solvent casting technique using aripiprazole as a model drug, different concentrations of isolated biopolymer from *Lagenaria siceraria*, and a standard polymer.

## Results

All formulations of aripiprazole were flexible, smooth, and transparent in nature, with a weight range from 23.73 to 34.48 mg, pH range from 7.27 to 7.39, and folding endurance of 94–116 times. The content uniformity was in the range of 97.2–98.6.

## Conclusion

In-vitro and in-vivo release shows FL2 as the best formulation. On the basis in-vitro and in-vivo drug release, FL2 was found to be best formulation showing mucoadhesivity (36 h),  $t_{50\%}$  of 2.5 h,  $t_{80\%}$  of 23.4 h, and having  $R^2$  value of 0.9923, best-fit model Higuchi matrix analyzed by BIT-SOFT 1.12. Moreover, it was observed that significant amount of drug reaches to the brain through soft palatal route through neural pathway.

## Keywords:

aripiprazole, biofilm former, bioflexy films, brain targeting, *lagenaria siceraria*

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## Introduction

Schizophrenia is a long-term brain disorder affecting more than 21 million people worldwide [1]. A number of drug molecules cannot enter into the brain because of their low lipid solubility and also they are not transported by specific carriers present in the blood–brain barrier [2]. Unfortunately, for this reason, most of the long-term brain diseases like depression, psychosis, autism, and schizophrenia remain untreated yet [3].

Aripiprazole is a second generation atypical antipsychotic that improves both positive and negative symptoms of schizophrenia, that is, depression and mania. These effects are associated with its partial agonistic activity at D2 receptors [4]. Aripiprazole is categorized under black box warning drugs, as it produces suicidal tendencies in specially pediatric and geriatric patients owing to its serious adverse effects. The elderly patients having psychosis when treated with aripiprazole have greater risk of death owing to cardiovascular collapse, infection, or stroke [5].

The soft palatal route is flexible, is highly vascularized, and has nonkeratinized stratified squamous epithelium,

and it is supposed to be 4–4000 times more permeable than skin [6]. It is innervated by cranial nerve V (i.e. lesser palatine nerve). The soft palatal delivery offers direct targeting of drug molecule into the brain through interneural and intraneural pathways [7].

The plant *Lagenaria siceraria* (Family: Cucurbitaceae) is commonly known as bottle gourd, is grown throughout the India, and is available in the market whole year. The phytochemistry of plant showed 2.5 g of carbohydrate, 0.2 g of protein, and 0.6 g of fiber per 100 g of edible portion. The fruit also contains vitamin B and ascorbic acid, water soluble polysaccharide, minerals, and amino acids [8].

Drug delivery through orosoft palatal route using bioadhesive dosage form such as bioflexy films is a novel route of drug delivery. Orossoft palatal mucosa is the site for administration of bioflexy films, and

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